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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/438,917	11/12/1999	PETER J WELCH	P-IU-3446	1019

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EXAMINER

HARRIS, ALANA M

ART UNIT	PAPER NUMBER
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1642

DATE MAILED: 09/30/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/438,917

Applicant(s)

WELCH ET AL.

Examiner

Alana M. Harris, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 May 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-10 is/are pending in the application.
- 4a) Of the above claim(s) 5-10 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 9. 6) ☐ Other: _____

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group III (claim 3) in Paper No. 19, received May 13, 2002 is acknowledged. The traversal is on the ground(s) that there is no serious burden to search the claims of Groups I-IV and VII. This is found partially persuasive. Groups I-IV will be examined together because as Applicants indicated in their Remarks to the restriction requirement because all the claimed nucleic acid sequences of Groups I-IV encode HTS1, a tumor suppressor molecule. However, the remainder of the restriction requirement set forth in Paper No. 18, mailed March 22, 2002 is maintained for the reasons set forth in the said paper.

The requirement is deemed proper and is therefore made FINAL.

2. Claims 1-10 are pending.

~~Claims 5-10, drawn to non-elected inventions are withdrawn from examination.~~

Claims 1-4 are examined on the merits.

Information Disclosure Statement

3. The information disclosure statement filed February 14, 2001 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because it improperly cites references on pages 2-4, which do not include dates of publication and furthermore are not provided. It has been placed in the application file, but the information referred to therein has not been considered as to the merits. Applicant is advised that the date of

any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609 ¶ C(1).

Drawings

4. The drawings are objected to because of reasons cited on attached form, PTO948 completed by the draftsman. Correction is required.

INFORMATION ON HOW TO EFFECT DRAWING CHANGES

5. Correction of Informalities -- 37 CFR 1.85

New corrected drawings must be filed with the changes incorporated therein. Identifying indicia, if provided, should include the title of the invention, inventor's name, and application number, or docket number (if any) if an application number has not been assigned to the application. If this information is provided, it must be placed on the front of each sheet and centered within the top margin. If corrected drawings are required in a Notice of Allowability (PTOL-37), the new drawings **MUST** be filed within the **THREE MONTH** shortened statutory period set for reply in the "Notice of Allowability." Extensions of time may NOT be obtained under the provisions of 37 CFR 1.136 for filing the corrected drawings after the mailing of a Notice of Allowability. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

6. Corrections other than Informalities Noted by Draftsperson on form PTO-948.

All changes to the drawings, other than informalities noted by the Draftsperson, **MUST** be made in the same manner as above except that, normally, a highlighted (preferably red ink) sketch of the changes to be incorporated into the new drawings **MUST** be approved by the examiner before the application will be

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allowed. No changes will be permitted to be made, other than correction of informalities, unless the examiner has approved the proposed changes.

Timing of Corrections

Applicant is required to submit acceptable corrected drawings within the time period set in the Office action. See 37 CFR 1.185(a). Failure to take corrective action within the set (or extended) period will result in **ABANDONMENT** of the application.

7. The drawings are objected to because figures 2 and 5 each contain only one figure description. However, Figure 2 has four panels that should be identified as Figure 2A-2D with accompanying figure descriptions and Figure 4 has six panels that should also be separately identified with figure descriptions.

Specification

8. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code on page 19, line 26. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable

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one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 1-4 are broadly drawn to substantially pure tumor suppressor molecules comprising:

- (a) several nucleotide sequences of SEQ ID NO: 2, 18 or 5;
- (b) at least fifteen contiguous nucleotides of said nucleotide sequences;
- (c) nucleic acid molecules encoding substantially the same amino acid sequences of SEQ ID NO: 6; and
- (d) functional fragments of said nucleic acid and amino acid molecules.

Applicants' have identified the nucleic acid sequences and the encoded polypeptide as human tumor suppressor-1 (HTS1). According to the specification the HTS1 molecules are intended to be used in the restoration of normal proliferative patterns in neoplastic cells, *in vivo* therapies geared toward treatment of cancer, as well as in diagnostic and prognostic assays relative to cancer, see pages 36, line 12-page 38, line 21; page 41, line 1-page 42, line 14 and page 43, lines 3-26.

However, Applicants' specification does not evidence the aforementioned intended uses of SEQ ID NO: 2, 18, 5 or 6, nor functional fragments and variant sequences encompassed by the substantially same claim language. The specification does not enable one of ordinary skill in the art to definitively assess the incidence of any type of cancer, such as the carcinomas and sarcomas listed on page 41, lines 15-22. The specification also does not enable one of ordinary skill in the art to implement fragments and variants of SEQ ID NO: 2, 18, 5 or 6 in diagnostic and prognostic assays

as asserted. There is no data presented supporting the effectiveness of full length sequences of SEQ ID NO: 2, 18, 5 and 6 in therapies. Consequently, the monitoring of effectiveness of therapies would be inconclusive and unreliable. There is insufficient evidence presented yielding discriminate and differential expression of HTS1 molecule, which could possibly support distinctions between normal and cancerous cells. In regard to the functional fragments and substantially the same nucleic and amino acid sequences there is no disclosure designating what changes to molecules could be tolerated enabling one of ordinary skill in the art to make and use the said sequences in any of the intended methods disclosed in the specification. The experimental design presented in the specification lacks information regarding the applicability of SEQ ID NO: 2, 18, 5 and 6 relative to cancer therapies, diagnostic and prognostic assays. Notwithstanding, given the differing pathologies of varying cancers it is not reasonable to conclude that each of the sequences and their functional fragment sequences would be effective in yielding a discriminate diagnosis and effective treatments.

Based on the analysis set forth it would require undue experimentation for the skilled artisan to practice this invention because there is no support in the specification for the enablement of the broadly claimed invention. Therefore, in view of the insufficient guidance in the specification, extensive experimentation would be required to enable the claims.

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 1-4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 1-4 recite "functional fragment" which is regarded as vague and indefinite. It is not clear from the claims what functions should a fragment of a tumor suppressor nucleic acid molecule or a tumor suppressor amino acid sequence should possess. Accordingly, the metes and bounds of the claims cannot be determined.

b. Claims 3 and 4 recite "substantially the same" which is vague and indefinite. It is not clear from the claims what is deemed substantially the same. Given the broadest interpretation it is reasonable to conclude that the claimed molecule of claim 3 could possibly share just 50 nucleic acids of SEQ ID NO: 5's 1664 base pairs.

Claim Rejections - 35 USC § 102

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application

being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

14. Claims 1 and 2 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent number 5,821,118 (filed April 24, 1995). Sequence 7, nucleic acid bases 14-28 of U.S. Patent #5,821,118 disclose a substantially pure tumor suppressor nucleic acid molecule comprising functional fragments of SEQ ID NO: 2 and SEQ ID NO: 18, see column 17 and attached database sheets.

15. Claims 1 and 2 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 97/46675 (December 11, 1997) or Accession number AAV10266 (June 3, 1998). Sequence 5 listed on pages 67-74 and Accession # AAV10266 discloses a substantially pure tumor suppressor nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO: 18 and a functional fragment of SEQ ID NO: 2.


16. Claims 1-4 are rejected under 35 U.S.C. 102(a) as being anticipated by WO 99/02675 (January 21, 1999) or Accession number AAX07369 (June 7, 1999). Nucleic acid sequences 902-916 in Figure 1a of the WO document and Accession #AAX07369 disclose a substantially pure tumor suppressor nucleic molecule comprising the nucleotide sequence of SEQ ID NO: 18. Both of these references also disclose a functional fragment of SEQ ID NO: 5 and SEQ ID NO: 2, see attached database sheets.

Applicants have stated on the record in the Remarks (paper #19), bridging paragraph of pages 2 and 3 and evidenced in Figures 6A and 6B that nucleic acid sequence, SEQ ID NO: 5 encodes HTS1, identified as amino acid sequence, SEQ ID NO: 6. Accordingly, the disclosed functional fragment of SEQ ID NO: 5 encodes a functional fragment of SEQ ID NO: 6.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (703) 306-5880. The examiner can normally be reached on 6:30 am to 4:00 pm, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, Ph.D. can be reached on (703) 308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4315 for regular communications and (703) 308-4315 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703)308-0196.

ALANA HARRIS
PATENT EXAMINER

Alana M. Harris, Ph.D.
August 12, 2002